

U.S.S.N 09/808,989
BRYAN ET AL.
PRELIMINARY AMENDMENT

IN THE CLAIMS:

Please replace claims 19, 26, 40, 47, 53, 58, 64, 67, 70, 73, and 74 with the following amended claims (a marked up copy of the amended claims are attached to this Amendment):

a42 19. (Amended) The composition of claim 17, wherein the bioluminescence generating system is selected from those isolated from: fireflies, *Mnemiopsis*, *Beroe ovata*, *Aequorea*, *Obelia*, *Vargula*, *Pelagia*, *Renilla*, *Pholas Aristostomias*, *Pachystomias*, *Porichthys*, *Cypridina*, *Aristostomias*, *Pachystomias*, *Malacosteus*, *Gonadostomias*, *Gaussia*, *Watensia*, *Halisturia*, Vampire squid, *Glyphus*, Mycotophids, *Vinciguerria*, *Howella*, *Florenciella*, *Chaudiodus*, *Melanocostus*, Sea Pens, *Chiroteuthis*, *Eucleoteuthis*, *Onychoteuthis*, *Watasenia*, cuttlefish, *Sepiolina*, *Oplophorus*, *Acanthophyra*, *Sergestes*, *Gnathophausia*, *Argyropelecus*, *Yarella*, *Diaphus*, *Gonadostomias* and *Neoscopelus*.

a43 26. (Amended) The combination of claim 24, wherein the component of the bioluminescence generating system comprises a luciferin.

a44 40. (Amended) The nucleic acid construct of claim 39, wherein the *Gaussia* luciferase is a *Gaussia princeps* luciferase.

a45 47. (Amended) The construct of claim 38, wherein the encoded luciferase and fluorescent protein comprise a fusion protein.

a46 53. (Amended) The fusion protein of claim 51, wherein the luciferase is a *Renilla reniformis* luciferase.

a47 58. (Amended) The nucleic acid construct of claim 57, comprising a sequence of nucleotides that encodes a ligand binding domain of a target protein.

a48 64. (Amended) A bioluminescence resonance energy transfer (BRET) system, comprising:

(a) a GFP encoded by the nucleic molecule of claim 1;

(b) a luciferase from which the GFP can accept energy when the GFP and luciferase associate; and

(c) a luciferin or other substrate of the luciferase.

67. (Amended) The BRET system of claim 65, wherein a conformational change in a modulator causes an increase in the proximity of the luciferase and GFP.

70. (Amended) A microelectronic device, comprising:

a substrate;

a plurality of micro-locations defined on the substrate, wherein each micro-location is for linking a macromolecule;

an independent photodetector integrated at or adjacent to each micro-location and optically coupled to each micro-location, each photodetector being configured to generate a sensed signal responsive to the photons of light emitted at the corresponding micro-location when a light-emitting chemical reaction occurs at that micro-location, each photodetector being independent from the photodetectors optically coupled to the other micro-locations; and

an electronic circuit coupled to each photodetector and configured to read the sensed signal generated by each photodetector and to generate output data signals therefrom that are indicative of the light emitted at each micro-location by the light-emitting chemical reactions, whereby the device detects photons of light emitted by light-emitting chemical reactions, wherein:

each micro-location is defined by a portion of the surface; and

the micro-locations defined on the substrate each comprise a component of a bioluminescence generating system and a green fluorescent protein of claim 1, whereby photons of light are emitted when a reaction takes place at that micro-location.

73. (Amended) The device of claim 71, wherein the bioluminescence generating system comprises a *Renilla reniformis* luciferase.

74. (Amended) A method of detecting and identifying analytes in a biological sample, comprising:

providing the microelectronic device of claim 70;

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attaching a macromolecule or plurality of different macromolecules to the surface at each micro-location on the device, wherein macromolecule is specific for binding to selected analyte that may be present in the biological sample;

contacting the sample with the surface of the microelectronic device, whereby any of the selected analytes that are present in the sample bind to the macromolecule attached to the surface at each micro-location;

exposing the surface of the microelectronic device to a second macromolecule or plurality thereof bound to the selected analyte already bound to the first macromolecule at each micro-location, wherein the second macromolecule comprises a component of a bioluminescence generating reaction;

initiating the bioluminescence generating reaction by contacting the surface of the device with the remaining components of the bioluminescence generating reaction, wherein the wavelength of the resulting light is shifted by the *Renilla reniformis* GFP; and

detecting photons of light emitted by the GFP using a photodetector optically coupled to each micro-location, each photodetector generating a sensed signal representative of the bioluminescence generation at the respective micro-location.

REMARKS

Any fees that may be due in connection with this application throughout its pendency may be charged to Deposit Account No. 50-1213.

The specification is amended to correct typographical and spelling errors and to produce grammatical clarity. The specification is also amended to add a definition of "TA" in the paragraph on page 39, lines 1-3. The basis for this amendment may be found in the specification of U.S. application Serial No. 08/908,909, which is incorporated by reference in the instant application and is apparent from the context in which "TA" is used throughout the specification of